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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/451,291	11/30/99	CHEN	L 07039-187001

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EXAMINER	
SOUAYA, I	
ART UNIT	**PAPER NUMBER**
1655	9

DATE MAILED: 05/07/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/451,291	Chen
Examiner	**Art Unit**
Jehanne Souaya	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 16, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above, claim(s) *6-10, 14-35, and 38-44* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-5, 11-13, 36, and 37* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3

18) ☒ Interview Summary (PTO-413) Paper No(s). 8

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Claims 6-10, 14-35, and 38-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8. An action on the merits of Claims 1-5, 11-13, and 36-37 follows.

Claim Rejections - 35 USC § 112

Enablement

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 11-13, and 36-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated DNA molecule that comprises a nucleic acid sequence that hybridizes under highly stringent conditions over the full length of the complement of a sequence that encodes a polypeptide with an amino acid sequence of SEQ ID NO:1 or SEQ ID NO: 3, wherein the nucleic acid sequence encodes a polypeptide with the ability to co-stimulate a T cell, to vectors and host cells comprising the nucleic acid sequence, and to methods

of producing a polypeptide encoded by the nucleic acid sequence, does not reasonably provide enablement for an isolated DNA comprising any nucleic acid sequence that encodes a polypeptide with the ability to co-stimulate a T cell, wherein the nucleic acid sequence hybridizes under stringent conditions to the complement of a sequence that encodes a polypeptide with an amino acid sequence with SEQ ID NOS: 1 or SEQ ID NO: 3, to vectors and host cells comprising the nucleic acid sequence, and to methods of producing a polypeptide encoded the nucleic acid sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are broadly drawn to any nucleic acid sequence that encodes a polypeptide with the ability to co-stimulate a T cell. The claims broadly encompass any functional fragment, variant, or homolog of SEQ ID NOS 1 and 3, however neither the specification, nor the art enable the skilled artisan to make or use the invention without undue experimentation. It is well established that to claim a chemical compound, such as a polynucleotide, the inventor must be able to define the compound so as to distinguish the compound from other materials. The claimed compound must be defined in terms so as to provide a permanent and definite idea of the complete and operative invention. In the instant case, the claimed polynucleotides have not been clearly defined in terms of structure and function, and therefore one cannot make and use the polynucleotides as claimed. As stated in Vaek (CAFC 20 USPQ2d 1438), the "specification must teach those of skill in the art how to make and use the invention as broadly as it is claimed."

However, in order to be able to make an invention, one must be able to clearly define that invention.

The specification sets forth that the invention is based on the cloning of human and mouse cDNA molecules encoding novel homologous molecules that co-stimulate the Tcell response of both species. The specification teaches that using PCR primers with sequences derived from an expressed sequence tag that had "significant" homology to human B7-1 and B7-2, a cDNA sequence that corresponded to an ORF (SEQ ID NO 2) was identified that encoded a novel B7-related molecule (p. 9). The specification teaches that the human polypeptide is designated hB7-H1 (SEQ ID NO 1) and the mouse polypeptide is mB7-H1 (SEQ ID NO 3) (see p. 1 of specification). The specification teaches that translation of the cDNA sequence (SEQ ID NO 2) indicated that the polypeptide (SEQ ID NO 1) it encoded is a type I transmembrane protein of 290 amino acids with contained an immunoglobulin "V-like" domain, Ig "C-like" domain, a transmembrane domain and a 30 amino acid cytoplasmic domain. The specification also teaches, however, that the extracellular domain of hB7-H1 only had 20 % amino acid identity with B7-1 and 15% with B7-2, and that the cytoplasmic domain was highly divergent from that of B7-1 and B7-2. Therefore, while hB7-H1 appears to be a homolog of B7 related sequences, it is unpredictable from the disclosure in the specification as to which molecules would be functional in costimulating T cells and also satisfy the broad structural requirements to which the claims are drawn. Furthermore, neither the specification nor the claims set forth any functional characteristics that are specific to hB7-H1 (ie: to particular domains) that a skilled artisan could

use to identify polynucleotides that constitute the B7 related polynucleotides of the claimed invention from other B7 related molecules, other than those described by SEQ ID NO. That is, it is unpredictable as to how the skilled artisan could modify the polypeptides of SEQ ID NO 1 or 3 without altering it's biological activity. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. Therefore, the citation of sequence homology results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks support regarding enablement. (See Russel et al, J. Mol. Biol. Vol. 244, 1994, pp 332-350, who teaches that the results of an analysis of side chain to side chain secondary structure and accessibility between related proteins suggest that there is little in common between distantly related protein structures and that secondary structure lengths and loops in distantly related structures vary substantially- p. 345).

The specification teaches that B7-H1 family genes or proteins encompass molecules which are from 50% to 98% identical to SEQ ID NOS 1 or 3 and encompass segments of molecules that from 30 to 865 nucleotides of SEQ ID NOS 2 or 4 (p. 11). Irrespective of how "% identity" is defined, it is clear that by any definition of "% identity", many sequences are encompassed by applicant's claims, and particularly those having "at least 50% identity" with fragments of the sequences taught in the specification, would bear little resemblance to the hB7-

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H1 nucleic acid sequence of the ~~claimed invention.~~ specification Furthermore, the specification does not define the degree of complementarity that is encompassed by the claim language.

In addition, in teaching the nucleic acid sequences of SEQ ID NOS 1-3, and the deduced amino acid sequences of the polypeptides they encode, applicant has not taught the isolation of a representative number of polynucleotides that fall within the scope of the large genus encompassed by the instant claims. Thus, while the teachings of the specification and of the prior art would enable a skilled artisan to make and use polynucleotides consisting of SEQ ID NO: 1-3 and *the complement* of SEQ ID NO: 1-3, it is unpredictable as to whether a skilled artisan could make and use an isolated DNA comprising any nucleic acid sequence that encodes a polypeptide with the ability to co-stimulate a T cell, wherein the nucleic acid sequence hybridizes under stringent conditions to the complement of a sequence that encodes a polypeptide with an amino acid sequence with SEQ ID NOS: 1 or SEQ ID NO: 3, to vectors and host cells comprising the nucleic acid sequence, and to methods of producing a polypeptide encoded the nucleic acid sequence. It would require undue experimentation for a skilled artisan to make and use the invention as broadly as it is claimed.

Written Description

4. Claims 1, 11-13, and 36-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any nucleic acid sequence that hybridizes under stringent conditions to the complement of a nucleic acid that encodes SEQ ID NOS 1 or 3, wherein the nucleic acid has the ability to co-stimulate a T cell. The claims, therefore broadly encompass any functional fragment, variant, or homolog of SEQ ID NO 1 and SEQ ID NO 3, however the specification has only taught sequences consisting of SEQ ID NOS 2 and 4 (nucleic acid sequences that encode the polypeptides of SEQ IDNOS 1 and 3 respectively). Furthermore, the specification does not define the degree of complementarity that is encompassed by the claim language. The specification teaches that B7-H1 family genes or proteins encompass molecules which are from 50% to 98% identical to SEQ ID NOS 1 or 3 and encompass segments of molecules that from 30 to 865 nucleotides of SEQ ID NOS 2 or 4 (p. 11). However, many sequences are encompassed by applicant's claims, and particularly those having "at least 50% identity" with fragments of the sequences taught in the specification, would bear little resemblance to the hB7-H1 nucleic acid sequence of the claimed invention. The claimed invention is drawn to a broad genus for which a representative number of sequences for each genus must be disclosed to meet the written description requirement of 112/1st paragraph. As set forth by the Court in *Vas Cath Inc. V. Mahurkar,* 19 USPQ2d 1111, the written description must convey to one of skill in the art "with reasonable clarity" that as of the filing date applicant was in possession of the claimed invention. There is not adequate description of the genus polynucleotides encompassed

by the instant claims. One of skill in the art would conclude that applicant was not in possession of the claimed nucleic acid sequences because the description of SEQ ID NOS 1 and 3 is of only 2 members of the possible nucleic acids that belong to this genus and is not representative of the homologs, variants, mutants and to the genomic sequences that contain these homologs, variants, and mutants to support the claims. Furthermore, the claims are only drawn to the functional limitation that these nucleic acid sequences have the ability to co-stimulate T cells. This does not further describe the large genus of polynucleotides encompassed by the broad structural limitations of the claims to the extent that SEQ ID NOS 1 and 3 would identify a representative number of members of the genus because B7-1 and B7-2 polypeptides have the ability to costimulate T cells, and are only 20% and 15% identical to hB7-H1 in their extracellular domain and their cytoplasmic domains were found to be highly divergent from that of hB7-H1. Thus the recitation of the functional limitation that the nucleic acids of the invention costimulate T cells still encompasses a large number of sequences that have not been described in the specification.

Indefinite

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-5, 11-13, and 36-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite in the recitation of "stringent conditions" as it is unclear what conditions the claims are drawn to. Stringency of hybridization conditions can be considered either "low", "moderate" or "high", encompass both salt concentration and temperature of hybridization, and determine the degree of complementarity needed for one nucleic acid molecule to hybridize to another. Absent such a definition the claims are indefinite as it cannot be determined what type of hybridization conditions are encompassed by the claims, and therefore, the degree of complementarity encompassed by the "nucleic acid sequence" which hybridizes to the complement of a nucleic acid sequence that encodes SEQ ID NO 1 or SEQ ID NO 3.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

8. Claims 1, 11-13, and 36-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Ostrand-Rosenberg et al (US Patent 5,858,776, filed 11/3/1993).

The claims are being interpreted broadly as it cannot be determined from the recitation in the claims the degree of complementarity between the "nucleic acid sequence" and the

complement of SEQ ID NOS 1 or 3. (See rejection made under § 35 USC 112/2nd paragraph in section 8). Ostrand-Rosenberg teaches an amino acid sequence (SEQ ID NOS 2 and 4) and their corresponding nucleic acid sequences (SEQ ID NOS 1 and 3 respectively) which, when expressed in tumor cells, are capable of costimulating T cells. The amino acid sequence of SEQ ID NO 2 in the '776 patent contains 23.9% similarity with SEQ ID NO 3 of the instant invention. The amino acid sequence of SEQ ID NO 4 of the '776 patent contains 22.1% similarity with the sequence of SEQ ID NO 1 of the instant invention. As it cannot be determined from the "stringent conditions" language of the claims of the instant invention, what degree of complementarity is encompassed by the language in those claims, the claims have been interpreted broadly, and the sequences taught by Ostrand-Rosenberg anticipate the instantly claimed invention.

9. No claims are allowable.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703)308-6565. The examiner can normally be reached Monday-Thursday from 7:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya

Jehanne Souaya
Patent examiner
April 30, 2001

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